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Nathaniel Heintz et al.

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For

Method of Performing Homologous Recombination Based Modification of

Nucleic Acids in Recombination Deficient Cells and Use of the Modified

Nucleic Acid Products Thereof

CERTIFICATE OF MAILING UNDER 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the ASSISTANT COMMISSIONER FOR PATENTS, U.S. PATENT AND TRADEMARK OFFICE, Washington, D.C. 20231 on 5 August 2002.

Betty Schultz

(Name)

RESPONSE AND AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS WASHINGTON, DC 20231

Sir:

In response to the Office action issued 26 June 2002, please replace the paragraph at page 89, lines 11-20 of the specification, with the following amended paragraph:

Generation of Ru49 loss-of-function mice. The Ru49 genomic locus was mapped using four lambda phage clones and four BAC clones derived from 129 SvE strain of mice. The Targeting vector contained a 3.7 kb 5' arm and a 6 kb 3' arm in a pKSNT vector [Tybulewicz et al., Cell 65:1153-1163 (1991)]. ES cell selections were performed at The Rockefeller University Gene Targeting Facility. Initial typing was done by Southern blot using a 500 bp pair probe from the 5' region (Fig. 13a) yielding a 15kb wildtype allele and 11.5 targeted

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allele upon digestion with BamHI. Subsequent typing was done using PCR primers internal to

the neo gene and a second pair within the disrupted region (5' primer: 5'-

AAAGTCCTGCTGGCTCGGGAATC-3' (SEQ ID NO:1) and 3'primer: 5'-

GCCTCCTCTGCATTTCAGGG-3') (SEQ ID NO:2).